

PCT

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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| Applicant's or agent's file reference 1H189130 20 WO0 MLG | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416) | |
| International application No. PCT/EP 03/09315 | International filing date (day/month/year) 31.07.2003 | Priority date (day/month/year) 01.08.2002 |
| International Patent Classification (IPC) or both national classification and IPC C12Q1/34 | | |
| Applicant GIS BIO INTERNATIONAL et al. | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:
- I ☒ Basis of the opinion
 - II ☐ Priority
 - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the International application
 - VIII ☐ Certain observations on the international application

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| Date of submission of the demand 24.02.2004 | Date of completion of this report 10.11.2004 |
| Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | Authorized Officer Herrero, M Telephone No. +49 89 2399-8542  |

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/09315**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-21 as originally filed

Claims, Numbers

1-8 as originally filed

9-18 received on 29.10.2004 with letter of 28.10.2004

Drawings, Sheets

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
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International application No. **PCT/EP 03/09315**

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

see separate sheet

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-18 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-18 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-18 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

SECTION I

6. Additional observations

The amended Claims 9-18 filed with the letter dated 28.10.04 have their basis in the originally filed application, and therefore do not contravene Art. 34(2)(b) PCT.

SECTION V

2. CITATIONS AND EXPLANATIONS

- 2.1 The present application pertains to an assay of endoglycosidase enzyme activity employing a substrate which can be cleaved by an endoglycosidase of interest, for instance, by an enzyme having activity of the heparanase type. The assay relies on measuring a signal resulting from a close proximity transfer, e.g. from fluorescence resonance energy transfer, between two compounds (an acceptor and a donor) attached to the cleavable enzyme substrate. The hereby disclosed assay, which does not require any step of separation of the fragments derived from the enzyme activity, can be miniaturized and may be in particular useful in the context of the high throughput screening of molecule libraries.

The experimental results provided in the application (cf Examples 3-7) substantiate the applicability of the hereby described approach for determining endoglycosidase enzyme activity of the heparanase type in a sample, employing a homogeneous time-resolved fluorescence measurement method.

None of the prior art documents cited in the International Search Report discloses or suggests the possibility of assaying/detecting a glycolytic enzymatic activity based on a technical approach in which a signal generated from a close proximity transfer is measured.

It would therefore appear that present Claims 1-13 encompass methods for determining endoglycosidase enzyme activity in a sample/detecting a compound

capable of modulating endoglycosidase enzyme activity, which may be regarded as novel and non-obvious within the meaning of Arts. 33(2) and (3) PCT.

Moreover, having regard to the available prior art the compositions of independent Claims 14 and 15 and the kits according to Claims 16-18 would also appear to meet the novelty and inventive step criteria of Art. 33(2) and (3) PCT.

2.2 Further comments

- (i) The description provides technical support within the meaning of Art. 6 PCT for the performance of the hereby pursued endoglycosidase enzyme activity assays only insofar as the corresponding working approach is based on measuring the fluorescent signal emitted by an acceptor fluorescent compound, which results from the energy transfer between a donor fluorescent compound and said acceptor compound (see examples).

Hence the intended methods according to independent Claims 1 and 3 (and to part of dependent Claims 5, 6, 11 and 13), which rely on the measurement of a signal resulting from a transfer, via a close proximity transfer effect of any possible type (e.g. those referred to on page 4, lines 16-21 of the description), are not technically supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description (cf page 4, lines 22-34, bridging over pages 5-14 and Examples) and drawings (cf Figures 1-4).

- (ii) With respect to Claims 14, 15 and 16 it is noted that the use of expressions like "preferably" or "possibly" has no limiting effect on the scope of said claim, i.e. the feature(s) following such expressions is (are) to be regarded as entirely optional (cf PCT Guidelines, C-III, 4.6).